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| APPLICATION NO. | FILING DATE | HARLEY FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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HM12/0131

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| EXAMINER | |
|---|---|
| ZEMAN, M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| [illegible] | 35 |

DATE MAILED: 01/31/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 08/781,296 | HARLEY ET AL. | |
| | Examiner | Art Unit | |
| | Mary Zeman | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 July 2000 and 29 September 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *27-40* is/are pending in the application.

4a) Of the above claim(s) *30-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *27-40* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

## DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1631**.

Applicant's arguments filed 7/7/00 and 9/29/00 have been fully considered but they are not persuasive. Any non-reiterated rejections have been withdrawn.

Claims 27-40 are pending in this application. Claims 30-40 stand withdrawn from consideration as being non-elected with traverse.

### *Election/Restrictions*

Applicant has amended claims 27-29 to remove "immunogenic" from the claim, in order to "facilitate rejoinder" of the withdrawn claims. This amendment is not sufficient for rejoinder. As set forth in the previous office action, a method of predicting development of autoimmunity is a clearly separably patentable invention from a method of administering a composition. The peptide compositions of claims 30-34 are still patentably distinct from those of claims 27-29, as they require immobilization. An immobilized peptide, such as on a plate, cannot be administered to a patient, as required by claim 28. Therefore, the rejection stands, and is made FINAL.

This application contains claims 30-40 drawn to an invention nonelected with traverse in Paper No. 32. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Once any product claims are deemed allowable, Applicant may request the rejoinder of the subject matter of claims drawn to methods of using that same product. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

### *Claim Rejections - 35 USC § 112*

Claims 28 and 29 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments are not commensurate in scope with the claimed invention. As set forth previously, the specification provides limited results for particular epitopes of EBV under particular dosing schedules. The field of autoimmunity is so unpredictable, that one of ordinary skill in the art would not be able to exrapolate from the limited examples to the scope of the claims now pending. Applicant is simply providing an invitation to experiment with the large variety of peptides, dosages, and dosing schedules in order to find tolerance inducing regimes. As such, it would require undue experimentation for one of skill in the art to practice the invention, therefore, the specification is not enabling for the breadth of the pending claims.

Further, while any given specific peptide administered prior to EBV infection might elicit tolerance to EBV effects associated with *that particular peptide*, there is nothing to suggest that tolerance to an "epitope" of EBV confers tolerance to *all epitopes*. EBV is a large virus, with many proteins to which a patient may have an immune response. The specification fails to address this issue, and the declaration does not remedy that defect.

The data discussed in the declaration of record by Dr Harley seems to indicate the induction of tolerance to a *particular peptide* when the peptide is used for immunization under particular conditions or dosing schedules. The tolerance was measured by the lack of subsequent production of the relevant autoantibody to that peptide. There is no indication that immunization with one peptide tolerizes the subject to ALL of the potential autoantibody incuding epitopes on the EBNA molecule, or any other EBV antigenic protein. The claims are not limited to particular dosing schedules or the conditions set forth in the declaration, which appear to have a material effect upon the induction of tolerance to that antigen. Nor are the claims limited to inducing tolerance to solely the administered epitope.

The specification does not set forth any direct correlation between the administration of the elected composition, and the development of tolerance to EBV associated immune responses. While antibodies to a particular epitope could be common in a patient with SLE, there is no indication that the administration of a single epitope, would have any effect upon the clinical course of the disease, whether it be preventing the development of that disease, or the treatment of that disease. It is also not clear that the administration of the claimed composition would prevent the development of antibodies to other autoantigen epitopes when challenged with native virus. If there are so many epitopes, as set forth in claim 27, it is possible that despite the

vaccine with one epitope, the patient may develop antibodies to the a different epitioe upon challenge with native virus. Therefore, the specification is not enabling for the invention as it is now claimed.

*Claim Rejections - 35 USC § 102*

As has been set forth in previous Office Actions the claims are entitled to the filing date of the provisional application .

The exact limited peptide of SEQ ID NO:27 is free of the art, however, in view of the ambiguity of the claims any peptide or polypeptide containing SEQ ID NO: 27 is viewed as within the scope of the claim.

Claim 27 remains rejected under 35 USC §102 (e) as being clearly anticipated by Middeldorp (US 5, 965,353).

Middeldorp discloses SEQ ID NO: 1 which contains applicant's SEQ ID NO: 27 as being an immunogenic fragment. In addition, Middeldorp discloses SEQ ID NO:6 which corresponds exactly to applicant's SEQ ID NO: 24. Applicant attempts to distinguish from SEQ ID NO: 6 of Middeldorp, however, Applicant appears to be aligning two differing sequences. SEQ ID NO: 6 of Middeldorp has been copied from the image of the '353 patent as follows:

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Pro Gly Ala Ile Glu Gln Gly Pro Ala
1 5

MKB

< Pro Gly Ala Ile Glu Gln Gly Pro Ala

Applicant's sequence is also PRO GLY ALA ILE GLU GLN GLY PRO ALA, as clearly set forth in the response mailed 11/02/00. The examiner fails to see how these two peptides differ.

Claim 27 remains rejected under 35 USC §102(b) as being clearly anticipated by Middeldorp (WO 94/06912).

Applicant's arguments for this reference are the same as above, and are similarly not persuasive. Middeldorp (WO 94/06912) discloses SEQ ID NO:6 which corresponds exactly to applicant's SEQ ID NO: 24. Middeldorp specifically discloses the use of peptides or fragments of the peptides for use in treating EBV-related diseases (see page 9, third paragraph and page 11 first full paragraph).

### *Claim Rejections - 35 USC § 103*

Claims 28 and 29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Middeldorp (US Patent 5,965,353).

Applicant's arguments are not commensurate in scope with the pending claims. As set forth above, Middeldorp discloses the exact peptide recited in claims 28 and 29, and discloses the treatment of EBV-related disease with the disclosed peptides.

Claims 28 and 29 are rejected as being obvious over Middeldorp in view of the suggestion at column 4, lines 59-64 of Middeldorp to employ the recited peptides in the treatment of EBV-related disease. In this suggestion, pharmaceutical preparations of the peptides are contemplated. Middeldorp specifically includes the use of fragments of the peptides he discloses at column 5 line 36 to column 6 line 15- which includes the peptide which is identical to the instant SEQ ID NO: 24. The peptides to be used must contain at least one epitope. By immunizing a subject with a peptide, one tolerizes the subject to the effects of said peptide. Therefore, the suggestion of Middeldorp to immunize with peptides or fragments of SEQ ID Nos 1 and 6, renders the claimed invention *prima facie* obvious, barring evidence to the contrary.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

No claim is allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308 4028.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center receptionist whose telephone number is (703) 308-0196.

MARY K. ZEMAN
PATENT EXAMINER

mkz
January 22, 2001

MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1500~~
AU 1631